to advance the research and management of pain from chronic benign conditions and from cancer. This predominance is not surprising, as anesthesiologists are often called as consultants in pain management because of their expertise in narcotic pharmacology and neural blocking procedures. Anesthesiologists who get deeply involved in managing chronic pain, however, realize rapidly that occasional "nerve blocking" will not single-handedly solve a patient's pain problem. Therefore, more and more anesthesiologists have come out of the operating room to become "algologists" (from the Greek word *algos*, meaning pain), progressively involving themselves in the total physical and psychological management of patients with chronic pain.

To understand their role in managing cancer pain, anesthesiologists have to dispel some of the myths regarding the use of somatic therapies. Rarely is neural blocking or drug therapy effective as sole therapy. Neurolytic blocks and surgical rhizolysis are not permanent, and involvement with psychological factors is absolutely necessary. Somatic and psychological therapies must be simultaneously orchestrated to achieve maximum effect on the changing pain patterns that emerge with the progression of disease. Tailoring narcotic and nonnarcotic analgesics to each person's needs, the concomitant use of antidepressants and controlling side effects are the mainstays of therapy. Antidepressant drugs are required by most patients with cancer pain because of the high incidence of reactive depression, evidenced by their high scores in hysteria, depression and hypochrondriasis when tested with the Minnesota Multiphasic Personality Inventory. Combining a low-dose narcotic with a nonsteroidal anti-inflammatory drug such as ibuprofen, 600 mg, produces more analgesia compared with the same narcotic dose given alone, especially in patients with bone metastasis. The use of analgesics for chronic cancer pain differs from their use for acute pain. One has to respect the fact that tolerance with prolonged narcotic use is predictable and varies individually. Therefore, the use of a time-contingent, around-the-clock approach, tailoring the drug dose and frequency regimen to the individual patient, is mandatory for adequate pain control. Newer, longer-acting narcotics, such as MS Contin (the Purdue Frederick brand of morphine sulfate), diminish the need to take drugs frequently.

Neural blocking is generally resorted to only if intolerable side effects develop with analgesics, when the area of pain is local enough, when functions important to a patient will not be compromised with neurolytic block and when cognitive-behavioral factors will not negate the beneficial effect of block. Neurolytic blocks should not be done without a prior diagnostic local anesthetic block. Celiac plexus block and somatic nerve block must be done under fluoroscopy for precision.

Anesthesiologists should be aware of the indication for using recently introduced pain management techniques such as central and stimulation-produced analgesia and intrathecal and epidural opiates. Periventricular grey stimulation is known to induce endorphin release but plasma and cerebrospinal fluid specimens do not reveal a consistent increase of endorphins. An indication for this technique includes the presence of generalized pain, poor analgesia and intolerable side effects with narcotics. Recent studies in our institution (the University of California, Los Angeles) show that 13 of 17 patients who received periventricular grey stimulation withdrew themselves from narcotics within two weeks after the surgical procedure. Peripheral stimulation with transcutaneous nerve stimulation is limited to deafferentation pain and as an adjunct to pharmacologic tailoring. Postherpetic and postsurgical pain respond well to this treatment, in contrast to bone or neural compression pain. The subject of intrathecal and epidural opiates has been dealt with repeatedly in anesthesia literature. The main concern in using this modality in patients with chronic cancer pain is that, as with other routes, tolerance develops with epidural opiates with ongoing use and patients therefore require frequent dose adjustments.

THERESA FERRER-BRECHNER, MD
Los Angeles

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Bupivacaine Toxicity

In 1979 Albright described five cases of death resulting from accidental intravascular administration of long-acting amide local anesthetics, and the speculation was that bupivacaine hydrochloride is relatively more cardiotoxic than the shorter acting amide local anesthetic lidocaine. This speculation has been controversial and the subject of intense investigation.

In the past several years, extensive studies of bupivacaine cardiotoxicity have involved a variety of experimental models including isolated animal hearts, unanesthetized and unventilated mice, anesthetized and ventilated cats and dogs, awake monkeys and awake and unanesthetized dogs and sheep. Although the results of these studies have conflicted, it has become increasingly apparent that bupivacaine is more cardiotoxic than lidocaine. In conscious sheep, clinically equivalent doses of lidocaine and bupivacaine produce the expected toxic effects on the central nervous system with intravenous bolus injection. Serious cardiac arrhythmias develop with the use of bupivacaine, however, and not with lidocaine. When acute respiratory acidosis is induced in sheep just before administering a local anesthetic, bupivacaine, but not lidocaine, produces fatal cardiovascular collapse.

A possible mechanism for the differences in the cardiotoxicity of these two amide local anesthetics has been offered by Clarkson and Hondeghem. The electrophysiologic effects associated with bupivacaine and lidocaine were studied in guinea pig ventricular muscle with a voltage clamp technique to control membrane potential. Both local anesthetic agents block cardiac sodium channels during the upstroke of the action potential, but the recovery from block during diastole proceeds slowly with bupivacaine compared with lidocaine. Lidocaine rapidly enters and leaves the sodium channel;

bupivacaine, however, is a "fast-in, slow-out" agent. As a result of the slow recovery with the use of bupivacaine, a substantial frequency-dependent block accumulates at heart rates between 60 and 150 beats per minute (slow recovery from block during diastole). Bupivacaine is therefore more cardiotoxic than lidocaine at clinically equivalent local anesthetic concentrations; bupivacaine is potentially cardiotoxic when a large dose (probably 1 mg per kg of body weight or greater) is given intravascularly.

In August 1984, with an increasing number of reported deaths related to accidental intravascular bupivacaine injection, mostly among the obstetric population, the Food and Drug Administration issued urgent new recommendations about bupivacaine, stating that the 0.75% concentration is no longer recommended for obstetric anesthesia. The reason for the increased incidence of cardiotoxic reactions to bupivacaine in pregnancy is not clear. It may be due to the more frequent use of bupivacaine for obstetric epidural blocks or possibly that the physiologic changes during pregnancy make a woman more susceptible to such reactions, or more difficult to resuscitate, than a nonpregnant woman.

Despite its potential cardiotoxicity, bupivacaine remains a very useful agent for regional anesthesia, with a longer duration of action than lidocaine and, in lower concentrations, the ability to produce a high-quality analgesic block with minimal motor block. With careful administration and using meticulous techniques of test dosing and slow administration of a dose in fractional amounts, bupivacaine can be used effectively and safely. It is apparent, however, that great caution must be exercised to prevent an accidental intravascular injection of a large dose of bupivacaine, whatever the concentration.

MARK A. ROSEN, MD
San Francisco

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Hypokalemia and Potassium Administration in the Perioperative Period

PERIOPERATIVE HYPOKALEMIA has given anesthesiologists cause for concern due to the accepted relationship between low serum potassium levels and cardiac dysrhythmias. Two practices resulting from this concern have recently been questioned: automatic postponement of elective surgical procedures when a serum potassium level is below arbitrarily chosen levels, resulting in inconvenience to the patient and the surgical team and a pronounced increase in the cost of hospital care; second, aggressive intravenous replacement of potassium that in itself can precipitate serious morbidity and mortality.

Serum potassium levels reveal little information about the total body exchangeable potassium (representing 0.4% of the total body potassium). If a serum potassium concentration of 4.0 mEq per liter is considered normal, a potassium level of 3.0 mEq per liter reflects a 25% deficit of total body potassium. In a 70-kg adult, this represents 1,100 mEq of potassium, too great a deficit to replace rapidly with safety. Acute hypokalemia can be seen during anesthesia; for example, a decrease in a serum potassium level of 1 mEq per liter can result from hyperventilation that reduces the arterial carbon dioxide pressure from 45 torr to 25 torr, resulting in no loss of total body potassium and a 12-mEq transfer from the extracellular to the intracellular compartment of potassium ions. Replacement in this situation is unnecessary and carries the risk of a dangerously high serum potassium level being attained.

Studies by Vitez and colleagues of patients with chronic hypokalemia and by Allard and Cheek of patients with acute hypokalemia seen intraoperativelay both suggest that the dangers of hypokalemia in the perioperative period may have been overstated and may be less than that of iatrogenic hyperkalemia from overadministration or too rapid an administration of potassium.

The commonly accepted potassium levels for an elective operation (3.0 mEq per liter for chronic hypokalemia and 3.5 mEq per liter for hypokalemia and digitalis therapy) are arbitrary generalizations that the study of Vitez and associates would suggest are too high to routinely cancel surgical procedures. The interpretation of a single potassium level should be judged individually in light of the clinical situation within which it is found, and electrocardiographic evidence of hypokalemia should be elicited. If potassium is to be administered in a patient with chronic hypokalemia, it should ideally be given before the admission of the patient for an operation. If hypokalemic-related cardiac dysrhythmias occur and intravenous repletion of potassium is considered necessary, it should be administered in dilute solution through a central line at a maximum rate of 0.5 mEq per kg per hour with continuous electrocardiographic monitoring.

MARTIN W. ALLARD, MD
Loma Linda, California

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Malignant Hyperthermia Update

IN THE EARLY 1970s, malignant hyperthermia was the leading cause of anesthetic deaths, with an estimated mortality rate of 65% to 80%. By the mid-1980s mortality rates have dropped to below 5%. This dramatic change in statistics can be attributed to several factors: an awareness by the medical and lay community, with the increased detection of persons who might be susceptible to malignant hyperthermia; the early detection and treatment of malignant hyperthermia by anesthesiologists, and the availability (1979) of injectable dantrolene sodium, a drug that effectively reverses a malignant hyperthermia crisis.

Typically the syndrome is manifested by sinus tachycardia, a rising blood pressure and tachypnea. The skin becomes mottled—cyanotic with patches of bright red flushing. Rigor mortis-like stiffening of masseter or all skeletal muscles may develop. The temperature increase that results from the hypermetabolic condition in skeletal muscle occurs relatively